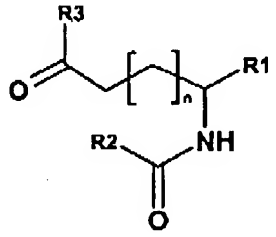
AMENDMENTS TO THE CLAIMS

The following Listing of Claims replaces all prior versions, and listings, of claims.

LISTING OF CLAIMS

1. (Currently Amended) A method for producing an N-acylated peptide, said method comprising:

a) reacting a peptide having at least one free amino group with an acylating agent of the general formula I



wherein

n is 0-8;

R^1 is $COOR^4$;

R^2 is a lipophilic moiety;

R^3 together with the carboxyl group to which R^3 is attached designate a reactive ester or a reactive N-hydroxy imide ester; and

R^4 is selected from the group consisting of hydrogen, C_{1-12}-alkyl and benzyl,

under basic conditions in an aqueous mixture containing less than 10 %w/w aprotic polar solvent; wherein the acylating agent is added to the reaction mixture as a solution in the aprotic polar solvent and the acylating agent/aprotic polar solvent solution is stabilized by the presence of an acid, wherein said acid is selected from the group consisting of sulphuric acid, methanesulphonic acid and trifluoroacetic acid; and

b) if R^4 in the acylating agent of step a) is not hydrogen, saponifying the acylated peptide ester group ($COOR^4$) under basic conditions; in order to produce said N-acylated peptide.

2. (Original) The method according to claim 1, wherein said reaction in step a) takes place in an aqueous mixture containing less than 8 %w/w aprotic polar solvent.

3. (Original) The method according to claim 1, wherein said reaction in step a) takes place in an aqueous mixture containing less than 5 %w/w aprotic polar solvent.

4. (Original) The method according to claim 1, wherein said reaction in step a) takes place in an aqueous mixture containing less than 3 %w/w aprotic polar solvent.

5. (Cancelled).

6. (Cancelled)

7. (Previously Amended) The method according to claim 1, wherein said aprotic polar solvent is selected from the group consisting of N-methyl-2-pyrrolidone, tetrahydrofurane and dimethylsulfoxide.

8. (Previously Amended) The method according to claim 1, wherein all of the aprotic solvent is added to the reaction mixture as the solvent for the acylating agent.

9. (Cancelled).

10. (Previously Amended) The method according to claim 1, wherein said acid is added to the aprotic polar solvent in a concentration from 0.01 %w/w to 1 %w/w.

11. (Previously Amended) The method according to claim 1, wherein said acid is added to the aprotic polar solvent in a concentration from 0.05 %w/w to 0.5 %w/w.

12. (Cancelled).

13. (Cancelled).

14. (Original) The method according to claim 1, wherein R^4 is hydrogen.

15. (Previously Amended) The method according to claim 1, wherein R^4 is selected from the group consisting of C_{1-8}-alkyl and benzyl.

16. (Original) The method according to claim 1, wherein R^3 together with the carboxyl group to which R^3 is attached designate a reactive N-hydroxy imide ester.

17. (Original) The method according to claim 1, wherein the acylated peptide ester is saponified in step b) at a pH value in the range of 10-14.

18. (Original) The method according to claim 1, wherein the acylated peptide ester is saponified in step b) at pH range from 9-13.

19. (Original) The method according to claim 1, wherein pH of the reaction mixture in step a) is from pH 9 to pH 13.

20. (Original) The method according to claim 1, wherein pH of the reaction mixture in step a) is from pH 10 to pH 12.

21. (Original) The method according to claim 1, wherein pH of the reaction mixture in step a) is from pH 11.0 to pH 11.5.

22. (Original) The method according to claim 1, wherein the temperature of the reaction

mixture in step a) is in the range of 0-50 °C.

23. (Original) The method according to claim 1, wherein the temperature of the reaction mixture in step a) is in the range from 5-40 °C.

24. (Original) The method according to claim 1, wherein the temperature of the reaction mixture in step a) is in the range from 10-30 °C.

25. (Previously Amended) The method according to claim 1, wherein R^2 is selected from the group consisting of C_{3-39}-alkyl, C_{3-39}-alkenyl, C_{3-39}-alkadienyl and steroidal residues.

26. (Original) The method according to claim 25, wherein R^2-C(=O)- is selected from the group consisting of lithocholoyl and hexadecanoyl.

27. (Previously Amended) The method according to claim 1, wherein said peptide used as starting material for step a) has a peptide purity of at least 80 as determined by RP-HPLC (reversed phase-high performance liquid chromatography).

28. (Original) The method according to claim 1, wherein said peptide used as starting material for step a) has a peptide purity of at least 90% as determined by RP-HPLC.

29. (Original) The method according to claim 1, wherein said peptide used as starting material for step a) has a peptide purity of at least 93% as determined by RP-HPLC.

30. (Original) The method according to claim 1, wherein said peptide used as starting material for step a) has a peptide purity of at least 95% as determined by RP-HPLC.

31. (Original) The method according to claim 1, wherein said peptide used as starting material for step a) has a peptide purity of at least 97% as determined by RP-HPLC.

32. (Previously Amended) The method according to claim 1, wherein said peptide is selected from the group consisting of glucagon-like peptide-1 (GLP-1), exendin-4, glucagon-like peptide-2 (GLP-2), glucagon, insulin, analogues thereof and derivatives of any of the foregoing.

33. (Original) The method according to claim 1, wherein said peptide is a GLP-1 agonist.

34. (Original) The method according to claim 1, wherein said peptide is selected from the group consisting of exendin-3, exendin-4, Arg^{34}-GLP-1(7-37), Gly^{8}-GLP-1(7-36)-amide, Gly^{8}-GLP-1(7-37), Val^{8}-GLP-1(7-36)-amide, Val^{8}-GLP-1(7-37), $Val^{8}Asp^{22}$-GLP-1(7-36)-amide, $Val^{8}Asp^{22}$-GLP-1(7-37) , $Val^{8}Glu^{22}$-GLP-1(7-36)-amide , $Val^{8}Glu^{22}$-GLP-1(7-37), $Val^{8}Lys^{22}$-GLP-1(7-36)-amide, $Val^{8}Lys^{22}$-GLP-1(7-37), $Val^{8}Arg^{22}$-GLP-1(7-36)-amide, $Val^{8}Arg^{22}$-GLP-1(7-37), $Val^{8}His^{22}$-GLP-1(7-36)-amide, $Val^{8}His^{22}$-GLP-1(7-37), des(B30)human insulin and analogues thereof.

35. (Previously Amended) The method according to claim 1, wherein said peptide is selected from the group consisting of
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPSKKKKKK-NH2 (ZP-10) and analogues thereof.

36. (Original) The method according to claim 1, wherein the reaction mixture in step a) comprises a buffer which is suitable for maintaining a substantially constant pH during the reaction.

37. (Original) The method according to claim 1, wherein said peptide is not insulin or an analogue thereof.